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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/808,774	03/15/2001	Mark T. Fisher	70009590-0020	5486

27910 7590 09/23/2003

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EXAMINER

SNEDDEN, SHERIDAN

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 09/23/2003

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/808,774

Applicant(s)

FISHER ET AL.

Examiner

Sheridan K Snedden

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 4-9, 11 and 20-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 10 and 12-19 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>9</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

1. This Office Action is in response to Paper #10, filed 27 June 2003. Applicant's amendment of claims 15 and 16 is acknowledged. Claims 4-9, 11, 20-39 are withdrawn from consideration. Claims 1-3, 10 and 12-19 are under examination.
2. Applicant argues that claims 1-19 and 20-39 should not be subject to a restriction. The traversal is on the ground(s) that there would be no burden imposed on the Examiner. This is not found persuasive because as the claims are directed to patentably distinct methods differing in both the steps and materials. The requirement is still deemed proper and is therefore made FINAL.

Withdrawal of Objections and Rejections

3. The objections and/or rejections not explicitly restated or stated below are withdrawn.

Drawings

4. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Information Disclosure Statement

5. Insofar as applicant filed an Information Disclosure Statement on 27 June 2003, one or more references appear to be missing and have been lined through and removed from consideration. These references would be considered upon resubmission.

Priority

6. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 17-19 of this application. No support is provided for method conditions that would control the oxidation/reduction in an anaerobic environment

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-3, 10, and 15-16 rejected under 35 U.S.C. 102(b) as being anticipated by Gorovits *et al.* (J Biol Chem. 1997 Jan 3;272(1):32-5). Gorovits *et al.* teach a DHFR refolding assay in which (a) the DHFR is first presented in an unfolded state, (b) GroEL is added to form the necessary chaperonin-DHFR complex, and (c) the chaperonin-DHFR complex was exposed to urea concentrations of less than 0.5M (see Materials and Methods; regarding claims 1-3, 10, and 15-16). The co-chaperonin GroES was also added in some experiments (regarding claim 12). Thus, the reference anticipates the claimed invention.

a. Applicant argues that the above reference teaches a method of "promoting the folding of said polypeptide from its unfolded to its folded state," and therefore does not teach the claimed invention. Applicant further adds, that the osmolyte urea was only present in residual amounts and did not promote the folding of DHFR.

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- b. Applicant's arguments have been fully considered but they are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., greater than residual amounts of urea) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The reference teaches a method that reads upon every step and material used in the claimed method and, thus anticipates the invention.
9. Claims 1-3, 10, 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Altamirano *et al.* (PNAS 1997 94: 3576-3578). Altamirano *et al.* teach a protein refolding assay in which (a) the protein is first presented in an unfolded state with a concentration of 8M urea, (b) then the protein is added to a gel column in which the chaperonin GroEL is immobilized in order to form the necessary chaperonin-protein complexes, and (c) the column is then washed with a refolding solution containing the osmolyte urea at concentrations of 2M (see Materials and Methods; regarding claims 1-3, 10, 14, 16). The concentration of 8M urea in the gel suspension would have been effective in reducing the aggregation of unfolding polypeptides and removal of this supernatant would have removed metastable polypeptide (regarding claim 13 and 15). Thus, the reference anticipates the claimed invention.

- a. Applicant argues that the osmolyte/chaperonin system is not the same as the fragmented "minichaperone system" taught by Altamirano *et al.* Applicant urges that the "minichaperone system" is inferior to the method of the present invention as

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demonstrated in the art and experiments with performed with malate dehydrogenase and citrate synthase. Applicant suggests that the folding described seen with “stringent protein substrates” in the method of Altamirano *et al.* can be explained by “permissive folding”. Applicant urges that the claimed invention is different due to the use of the oligomeric version of the chaperone which is superior to that of the reference because the oligomeric version may capture folding polypeptides or stabilize a metastable protein state for any length of time.

b. Applicant's arguments have been fully considered but they are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., oligomeric version; superior method which may capture folding polypeptides or stabilize a metastable protein state for any length of time) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The reference teaches a method that reads upon every step and material used in the claimed method and, thus anticipates the invention.

11. Claims 1-3, and 12-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Altamirano *et al.* (Nat Biotechnol. 1999 Feb;17(2):187-91). Altamirano *et al.* teach a protein refolding assay in which (a) the protein Cn5 toxin is first presented in an unfolded state, (b) then the protein is mix with a refolding matrix containing the chaperonin GroEL and the co-chaperonin DsbA immobilized on PPI-agarous, and (c) the column is then washed with a

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refolding solution containing the osmolyte arginine and the redox agent GSH (see Materials and Methods; regarding claims 1-3, 12, 14, and 19). The assay is conducted under an inert Argon atmosphere in order to control the oxidation/reduction in an anaerobic environment (see page 190, second column; regarding claims 17-18). The incubation with the GroEL agarous gels and removal of the supernatant is effective in reducing the aggregation of unfolding polypeptides and removal of this supernatant would have removed metastable polypeptide (see abstract; regarding claim 13 and 15). Altamirano *et al.* discusses the difficulty in refolding the Cn5 toxin and would have not been successfully refolded without the combination of all steps in the method (see page 187-188; regarding claim 16). Thus, the reference anticipates the claimed invention.

a. Applicant argues that the osmolyte/chaperonin system is not the same as the fragmented “minichaperone system” taught by Altamirano *et al.* Applicant urges that the “minichaperone system” is inferior to the method of the present invention as demonstrated in the art and experiments with performed with malate dehydrogenase and citrate synthase. Applicant suggests that the folding described seen with “stringent protein substrates” in the method of Altamirano *et al.* can be explained by “permissive folding”. Applicant urges that the claimed invention is different due to the use of the oligomeric version of the chaperone which is superior to that of the reference because the oligomeric version may capture folding polypeptides or stabilize a metastable protein state for any length of time.

b. Applicant's arguments have been fully considered but they are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e.,

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oligomeric version; superior method which may capture folding polypeptides or stabilize a metastable protein state for any length of time) are not recited in the rejected claim(s).

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The reference teaches a method that reads upon every step and material used in the claimed method and, thus anticipates the invention.

Conclusion

12. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan K Snedden whose telephone number is (703) 305-4843. The examiner can normally be reached on Monday - Friday, 8:30 AM to 5:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone number for regular communications to the organization where this application or proceeding is assigned is (703) 746-3975.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SKS
September 22, 2003

SKS

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
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